

I. FURTHER OBSERVATIONS ON THE VARIATIONS IN THE NUMBER OF LEUCOCYTES AND CRESCENTS IN MALARIA

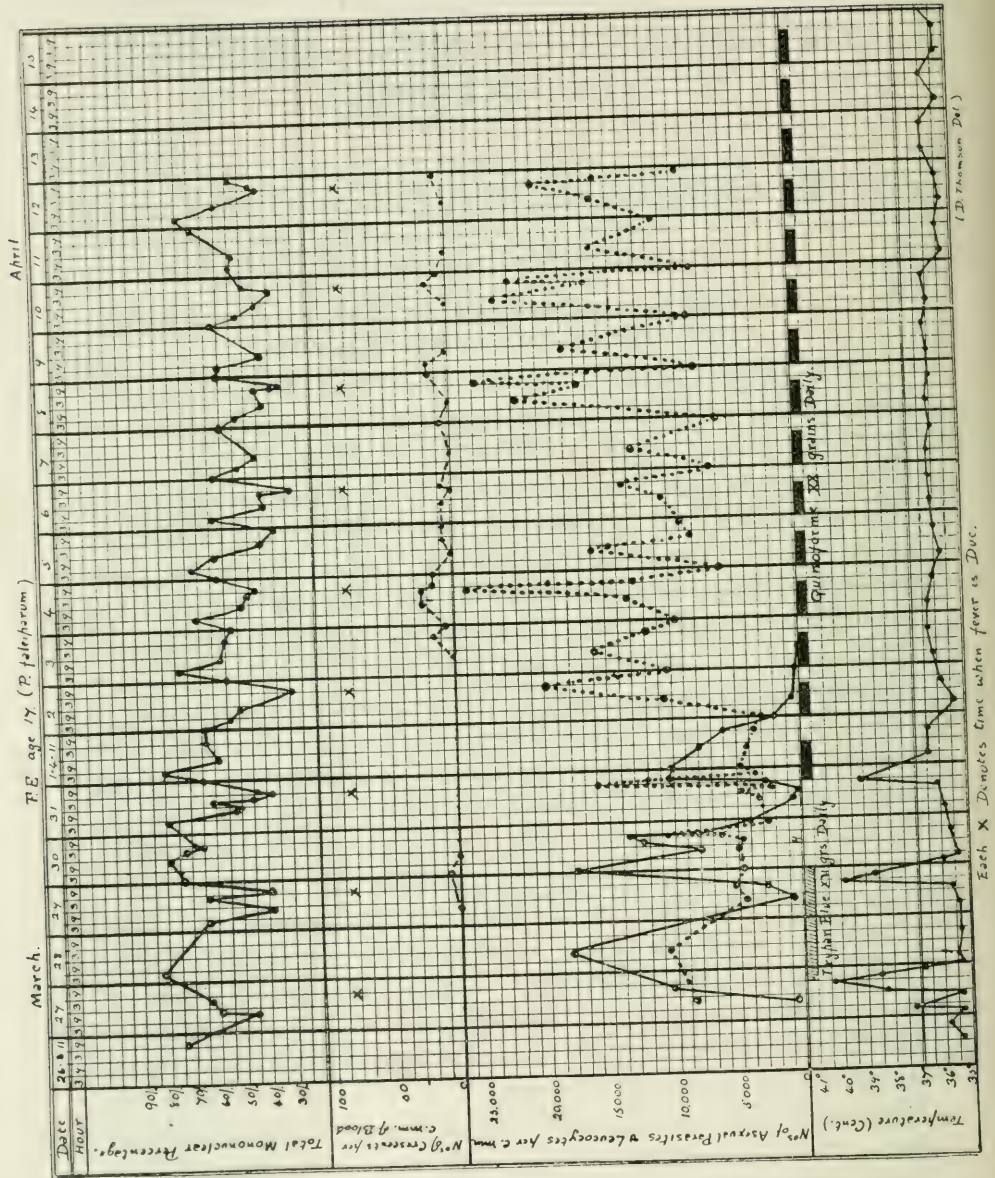
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(Received for publication 22 May, 1912)

(a) VARIATIONS IN THE NUMBER OF LEUCOCYTES IN CASES OF APPARENTLY CURED MALARIA

In a previous paper (Thomson, 1911) it was pointed out that, after a case of malaria had been apparently cured by quinine, the leucocytes began to vary in number in a remarkable manner. This phenomenon begins to show itself about one to two weeks after the disappearance of the parasites. In some cases it occurs earlier, in others later. About the time of the day at which the fever paroxysm had formerly occurred, the leucocytes showed a marked but transient increase, the polymorphs playing the greater part in this increase. I have now some slight reason to believe that this phenomenon is due to a small number of parasites, too scarce to be detected, sporulating about the same time as when they were numerous. On first thought, therefore, one would expect that this late leucocytic variation would be quotidian, tertian, or irregular in type, according as the fever was before it. I have found, however, that it is much more often quotidian and irregular in type than tertian. In fact, the case F. E. (*P. falciparum*), see chart, is about the only one I have noted so far which shows a tertian tendency in this leucocyte swing. When one considers, however, that an absolutely pure case of tertian infection is practically never found, it is not surprising that one seldom gets a case in which the leucocytes show a pure tertian swing. Cases in which the temperature curve shows a pure tertian type are common enough, but in these cases, if one examines the blood carefully, one finds that a few parasites sporulate between times, and these are sufficient to produce a variation in the total mononuclear percentage, although



not sufficient in number to produce a temperature. I think that this is why cases which are apparently purely tertian from the temperature curve, show a quotidian variation in the number of leucocytes later on.

In order to support my belief that a large number of malarial parasites on sporulating cause a leucopenia, whereas a small number on sporulating cause a leucocytosis, I have tried the effect of hypodermic injections of dead malarial parasites on the leucocytes, on twelve occasions. My technique was as follows:— Having ascertained the number of parasites per c.mm. of blood in a case of malaria during a paroxysm, I drew off several cubic centimetres of blood from a vein into an equal volume of citrate solution in a sterile syringe. This was transferred to a sterile vessel and carbolic acid added so as to make a 1 % strength. This was left in the cold for a few days, so as to ensure the death of the parasites. By injecting hypodermically a given volume of this material into a person, one was able to watch the effect on the leucocytes of a given number of dead parasites.* A leucocyte count was made immediately before the injection, and two to three more counts made at half-hour intervals afterwards.

In three of these twelve experiments I injected three, four and five millions of malignant tertian parasites, respectively, and got a slight increase in the number of leucocytes in one half to one hour afterwards.

In three more I injected doses of thirty to forty millions, and obtained a slight decrease in the number of leucocytes.

On five occasions I injected from ten to twenty millions, and obtained a marked increase of leucocytes in three of these in one half to one hour after the injection.

The remaining experiment was an injection of five million benign tertian parasites, taken during a rigor. This resulted in a slight increase of leucocytes in half an hour.

It would therefore appear that it requires an injection of ten to twenty million malignant tertian parasites to cause a leucocytosis, whereas numbers from thirty to forty million and upwards cause a leucopenic effect (as in a malarial paroxysm). On one

* The material was mixed with sterile water before injection, so as to haemolyse the corpuscles so that the poisonous effect of the parasites, might be more rapid.

occasion the latter number caused a slight rigor, but no increase of temperature. During a malarial paroxysm there is as a rule an accompanying leucopenia; some observers, however (Stephens and Christophers, 1908), have described a transient leucocytosis lasting about twenty minutes just at the very commencement of the rigor. I have noticed this on two occasions only, and think that it may be explained by the supposition that a very few parasites sporulate before the majority of them, and these few cause the temporary leucocytosis, which soon becomes a leucopenia when the majority sporulate.

In cases of comatose malaria (malig. tert.) one frequently finds a marked leucocytosis during the fever paroxysm. I am quite unable to explain this exception. Recently I observed a leucocytosis of 80,000 per c.mm. in a case of uncomplicated comatose malaria four hours before death.*

(b) FURTHER REMARKS

A. Scherschmidt (1912) has partially confirmed the occurrence of a periodic post-malarial leucocytosis in nine out of twenty-three cases of malaria, or only in about one-third. His work has evidently been very thorough, as he took blood counts almost continuously at intervals of one hour, but in the majority of his twenty-three cases these were taken between 10 a.m. and 4 p.m., and only on a few isolated days did he examine as late as 8 p.m. He therefore only observed the leucocytes during a six-hours period of the day. I feel sure that he would have got better results by examining the blood as I stated, every four to six hours. I examined the blood of my cases at such intervals between 10 a.m. and 12 midnight, that is to say, I examined over a fourteen-hour period of the day as against the six-hour period of Scherschmidt.

On the first day of observation one should make a blood count at, say, 10 a.m., 2 p.m., 6 p.m., and 12 midnight. Next day make counts at 9 a.m., 12 mid-day, 4 p.m., and 8 p.m. By varying the times daily in this way, one hits upon the time at which the leucocytosis occurs. When this is found, three counts daily should enable one to bring out the variation on subsequent days. I think

* The post mortem did not reveal any complication.

that Scherschmidt has unfortunately mistaken my meaning, as he examined the blood of his cases every hour for a period of four to six hours, instead of at intervals of four to six hours. It is not necessary to examine the blood every hour, as the leucocytosis as a rule lasts for several hours. In a few of his cases, Scherschmidt commenced his blood counts too soon after the disappearance of the parasites. It is best to wait for seven to fourteen days after the parasites have apparently gone, due to the influence of the quinine treatment. Again, in two of his cases there was a more or less continuous leucocytosis throughout his daily four to six hours period of examination. It is quite probable that this period was the time of the post-malarial leucocytosis, and had he made a count at 12 midnight, it might have revealed the fall to normal. Scherschmidt used the Thoma Zeiss method of counting. The method I adopted was much more suitable for this work, as by means of a special pipette (Thomson, 1911) I was able to take samples of blood rapidly and leave over the counting of leucocytes in these samples till convenient. A differential count could also be made on these samples. Continued observations as above are, however, very trying, whatever method may be used, and I think that Scherschmidt deserves much credit for his laborious work.

Before proceeding to the consideration of the crescents, I would like to call special attention to chart of Case F. E. (*P. falciparum*), as it shows two points of importance very clearly.

(1) It shows how the asexual parasites leave the peripheral circulation before the sporulation and rise of temperature. This peculiarity of malignant tertian was first pointed out by Marchiafava and Bignami.

(2) It shows how the total mononuclear leucocyte percentage varies inversely with the temperature.

Further, it will be noticed that trypan blue in doses of twelve grains daily had little or no curative effect, whereas Quinoforme, a basic formate of quinine (French preparation) proved very satisfactory.

(c) VARIATIONS IN THE NUMBER OF CRESCENTS

In a previous paper (Thomson, 1911) it was stated that the crescents come into the peripheral circulation in outbursts from the inner organs (spleen and bone marrow), daily, every other day, or irregularly, according as the fever ten days previously had been quotidian, tertian, or irregular. At that time I had only observed this phenomenon occurring daily and irregularly; in fact, it is most commonly irregular, as malignant tertian malaria in the majority of cases is irregular in type. Classical tertian or quotidian cases are much more rare. I am now able to record a case which showed tertian outbursts of crescents following upon a tertian case of *P. falciparum* (see accompanying chart H. J.). This chart shows four distinct tertian outbursts of crescents. It also shows how quinine (thirty grains daily) very gradually reduces the number of crescents till they can no longer be detected.

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